

In the Specification

Please substitute the following paragraph at page 1, beginning at line 5:

This application is a continuation-in-part of Provisional Application Serial No. 10/114,718, filed Dec. ~~23~~24, 1998 and is hereby incorporated by reference in its entirety.

Please substitute the following paragraph at page 34, beginning at line 2:

X is selected from the group consisting of methylexnoxycarbonyl, and furan-2,5-diyl, and pharmaceutically acceptable salts and prodrugs thereof. More preferred are such compounds wherein A" is  $\text{-NH}_2$ , X is furan-2,5-diyl, and B" is  $\text{-S(CH}_2)_2\text{CH}_3$ ; wherein A" is  $\text{-NH}_2$ , X is furan-2,5-diyl, and B" is  $\text{-CH}_2\text{-CH(CH}_3)_2$ ; wherein A" is  $\text{-NH}_2$ , X is furan-2,5-diyl, and B" is  $\text{-COOEt}$ ; wherein A" is  $\text{-NH}_2$ , X is furan-2,5-diyl, and B" is  $\text{-SMe}$ ; or wherein A" is  $\text{-NH}_2$ , X is methyleneoxycarbonyl, and B" is  $\text{-CH(CH}_3)_2$ .

Please substitute the following paragraph at page 41, beginning at line 1:

Preferred  $\text{X}^2$  groups include  $\text{-CF}_2\text{-}$ ,  $\text{-CH}_2\text{-}$ ,  $\text{-OC(O)-}$   ~~$\text{-OC(O)-}$~~ ,  $\text{-OCH}_2\text{-}$ ,  $\text{-SCH}_2\text{-}$ ,  $\text{-NHCH}_2\text{-}$ , and  $\text{-N(C(O)CH}_3\text{)-CH}_2\text{-}$ . More preferred are  $\text{-OCH}_2\text{-}$ ,  $\text{-SCH}_2\text{-}$ , and  $\text{-N(C(O)CH}_3\text{)-CH}_2\text{-}$ . Most preferred is  $\text{-OCH}_2\text{-}$ .

Please substitute the following paragraph at page 48, beginning at line 6:

$\text{A}^2$  is selected from the group consisting of  $\text{-NR}^8$ ,  $\text{NHSO}_2\text{R}^3$   ~~$\text{-NHSO}_2\text{R}^3$~~ ,  $\text{-OR}^5$ ,  $\text{-SR}^5$ , halogen, lower alkyl,  $\text{-CON(R}^4)_2$ , guanidine, amidine,  $\text{-H}$ , and perhaloalkyl;

Please substitute the following paragraph at page 74, beginning at line 1:

Preferred  $\text{X}^2$  groups include  $\text{-CF}_2\text{-}$ ,  $\text{-CH}_2\text{-}$ ,  $\text{-OC(O)-}$   ~~$\text{-OC(O)-}$~~ ,  $\text{-OCH}_2\text{-}$ ,  $\text{-SCH}_2\text{-}$ ,  $\text{-NHCH}_2\text{-}$ , and  $\text{-N(C(O)CH}_3\text{)-CH}_2\text{-}$ . More preferred are  $\text{-OCH}_2\text{-}$ ,  $\text{-SCH}_2\text{-}$ , and  $\text{-N(C(O)CH}_3\text{)-CH}_2\text{-}$ . Most preferred is  $\text{-OCH}_2\text{-}$ .

Please substitute the following paragraphs at page 98, beginning at line 5 through to page 99, line 6:

Variable A moieties are assigned the following numbers:

|    | 1                        | 2 | 3  | 4  |
|----|--------------------------|---|----|----|
| A= | $\text{NH}_2\text{NH}_2$ | H | Me | Cl |

Variable B moieties are assigned the following numbers:

|    | 1  | 2    | 3    | 4      | 5    | 6    | 7    | 8  |
|----|--|------|------|--------|------|------|------|--|
| B= | <del>-SCH<sub>3</sub></del><br><u>-SCH<sub>3</sub></u> | -iBu | -cPr | -S-nPr | -SEt | -iPr | -nPr | <del>-CH<sub>2</sub>cPr</del><br><u>-CH<sub>2</sub>cPr</u> |

Variables Q<sup>1</sup> and Q<sup>2</sup> are divided into three groups, each listing eight different substitutes.

Q<sup>1</sup> and Q<sup>2</sup> moieties are assigned the following numbers:

Group 1:

**Q<sup>1</sup> and Q<sup>2</sup>**

1. -NH-CH<sub>2</sub>-C(O)R<sub>14</sub><sup>14</sup>
2. -NH-CH(CH<sub>3</sub>)<sub>3</sub>-C(O)R<sub>14</sub><sup>14</sup>
3. -NH-C(CH<sub>3</sub>)<sub>2</sub>-C(O)R<sub>14</sub><sup>14</sup>
4. -NH-C(CH<sub>3</sub>)<sub>2</sub>CH<sub>2</sub>-C(O)R<sub>14</sub><sup>14</sup>
5. -NH-CH(CH(CH<sub>3</sub>)<sub>2</sub>)-C(O)R<sub>14</sub><sup>14</sup>
6. -NH-CH(CH<sub>2</sub>(CH(CH<sub>3</sub>)<sub>2</sub>)))C(O)R<sub>14</sub><sup>14</sup>
7. -NH-CH(CH<sub>2</sub>CH<sub>2</sub>SCH<sub>3</sub>)<sub>3</sub>-C(O)R<sub>14</sub><sup>14</sup>
8. -NH-CH(CH<sub>2</sub>SCH<sub>2</sub>Ph)-C(O)R<sub>14</sub><sup>14</sup>

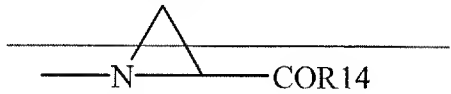
Group 2:

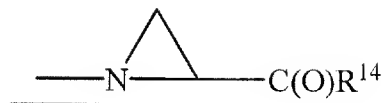
**Q<sup>1</sup> and Q<sup>2</sup>**

1. -NH-CH<sub>2</sub>CH<sub>2</sub>-C(O)R<sub>14</sub><sup>14</sup>

2.  $-\text{NH}-\text{CH}(\text{CH}_2\text{CH}_2\text{COR}^{14})-\text{C}(\text{O})\text{R}^{14}$
3.  $-\text{NH}-\text{CH}(\text{CH}_2\text{COR}^{14})-\text{C}(\text{O})\text{R}^{14}$
4.  $-\text{NH}-\text{CH}(\text{CH}_2\text{CONH}_2)-\text{C}(\text{O})\text{R}^{14}$
5.  $-\text{NH}-\text{CH}(\text{COR}^{14})\text{CH}_2-\text{C}(\text{O})\text{R}^{14}$
6.  $-\text{NH}-\text{CH}(\text{CH}_2\text{OR}^{17})-\text{C}(\text{O})\text{R}^{14}$
7.  $-\text{NH}-\text{CH}(\text{CH}_2\text{CH}_2\text{COR}^{14})-\text{C}(\text{O})\text{R}^{14}$
8.  $-\text{NH}-\text{CH}(\text{CH}_2\text{OH})-\text{C}(\text{O})\text{R}^{14}$

Group 3:**Q<sup>1</sup> and Q<sup>2</sup>**

1.  $-\text{NH}-\text{CH}(\text{CH}_2-\text{C}_6\text{H}_5\text{OH})-\text{C}(\text{O})\text{R}^{14}$
2.  $-\text{NH}-\text{C}(\text{c-propyl})-\text{C}(\text{O})\text{R}^{14}$
3.  $-\text{NH}-\text{C}(\text{c-pentyl})-\text{C}(\text{O})\text{R}^{14}$
4.  $-\text{NH}-\text{C}(\text{c-hexyl})-\text{C}(\text{O})\text{R}^{14}$
5.  $-\text{NH}-\text{CH}(\text{CH}_2\text{Ph})-\text{C}(\text{O})\text{R}^{14}$
6.  $-\text{N}(\text{CH}_3)-\text{CH}_2-\text{C}(\text{O})\text{R}^{14}$
7. 



8.  $-\text{NR}^{18}\text{R}^{19}$

where R<sup>4</sup> is selected from the groups consisting of OMe, OEt, OBn, O-*t*Bu, O-*n*Pr, OPh, -N(Me)<sub>2</sub>, morpholine, SMe, SEt; R<sup>17</sup> is methyl, ethyl, benzyl, and propyl; R<sup>18</sup> is H, Me, Et, Bn, Pr and Ph and R<sup>19</sup> is Me, Et, Bn, Pr and Ph; R<sup>18</sup> and R<sup>19</sup> is morpholinyl and pyrrolidinyl.

Please substitute the following paragraphs at page 100, beginning at line 17 through to page 101, line 6:


1.  $-\text{NH}-\text{CH}_2-\text{C}(\text{O})\text{R}^{14}$
2.  $-\text{NH}-\text{CH}(\text{CH}_3)-\text{C}(\text{O})\text{R}^{14}$
3.  $-\text{NH}-\text{C}(\text{CH}_3)_2-\text{C}(\text{O})\text{R}^{14}$
4.  $-\text{NH}-\text{C}(\text{CH}_3)_2\text{CH}_2-\text{C}(\text{O})\text{R}^{14}$

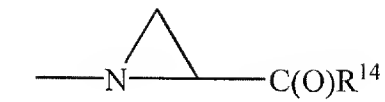
5.  $-\text{NH}-\text{CH}(\text{CH}(\text{CH}_3)_2)-\text{C}(\text{O})\text{R}_{14}^{14}$
6.  $-\text{NH}-\text{CH}(\text{CH}_2(\text{CH}(\text{CH}_3)_2))-\text{C}(\text{O})\text{R}_{14}^{14}$
7.  $-\text{NH}-\text{CH}(\text{CH}_2\text{CH}_2\text{SCH}_3)-\text{C}(\text{O})\text{R}_{14}^{14}$
8.  $-\text{NH}-\text{CH}(\text{CH}_2\text{SCH}_2\text{Ph})-\text{C}(\text{O})\text{R}_{14}^{14}$

Group 2:**Q<sup>1</sup> and Q<sup>2</sup>**

1.  $-\text{NH}-\text{CH}_2\text{CH}_2-\text{C}(\text{O})\text{R}_{14}^{14}$
2.  $-\text{NH}-\text{CH}(\text{CH}_2\text{CH}_2\text{COR}_{14}^{14})-\text{C}(\text{O})\text{R}_{14}^{14}$
3.  $-\text{NH}-\text{CH}(\text{CH}_2\text{COR}_{14}^{14})-\text{C}(\text{O})\text{R}_{14}^{14}$
4.  $-\text{NH}-\text{CH}(\text{CH}_2\text{CONH}_2)-\text{C}(\text{O})\text{R}_{14}^{14}$
5.  $-\text{NH}-\text{CH}(\text{COR}_{14}^{14})\text{CH}_2-\text{C}(\text{O})\text{R}_{14}^{14}$
6.  $-\text{NH}-\text{CH}(\text{CH}_2\text{OR}_{17}^{17})-\text{C}(\text{O})\text{R}_{14}^{14}$
7.  $-\text{NH}-\text{CH}(\text{CH}_2\text{CH}_2\text{COR}_{14}^{14})-\text{C}(\text{O})\text{R}_{14}^{14}$
8.  $-\text{NH}-\text{CH}(\text{CH}_2\text{OH})-\text{C}(\text{O})\text{R}_{14}^{14}$

Group 3:**Q<sup>1</sup> and Q<sup>2</sup>**

1.  $-\text{NH}-\text{CH}(\text{CH}_2-\text{C}_6\text{H}_5\text{OH})-\text{C}(\text{O})\text{R}_{14}^{14}$
2.  $-\text{NH}-\text{C}(\text{c-propyl})-\text{C}(\text{O})\text{R}_{14}^{14}$
3.  $-\text{NH}-\text{C}(\text{c-pentyl})-\text{C}(\text{O})\text{R}_{14}^{14}$
4.  $-\text{NH}-\text{C}(\text{c-hexyl})-\text{C}(\text{O})\text{R}_{14}^{14}$
5.  $-\text{NH}-\text{CH}(\text{CH}_2\text{Ph})-\text{C}(\text{O})\text{R}_{14}^{14}$
6.  $-\text{N}(\text{CH}_3)-\text{CH}_2-\text{C}(\text{O})\text{R}_{14}^{14}$
7. 



8.  $-\text{NR}_{18}^{18}\text{R}_{19}^{19}$

Please substitute the following paragraph at page 102, beginning at line 13:

where R<sup>4</sup> is selected from the groups consisting of OMe, OEt, OBn, O-*i*Bu, O-*n*Pr, OPh, -N(Me)<sub>2</sub>, morpholine, SMe, SEt; R<sup>17</sup> is methyl, ethyl, benzyl, and propyl; R<sup>18</sup> is H, Me, Et, Bn, Pr and Ph and R<sup>19</sup> is Me, Et, Bn, Pr and Ph; R<sup>18</sup> and R<sup>19</sup> is morpholinyl and pyrrolidinyl.

Please substitute the following paragraph at page 231, beginning at line 22:

Step B. 2-Diethylphosphonomethoxy-5-bromonitrobenzene was subjected to Step B of Example 37, Step B of Example 36, and Step D of Example 34 to give 2-amino-7-bromo-6-thiocyanato-4-phosphonmethoxybenzothiazole (38.1). mp >250°C(dec.). Anal. Calcd. for ~~C<sub>9</sub>H<sub>7</sub>N<sub>3</sub>O<sub>4</sub>PS<sub>2</sub>Br~~: C<sub>9</sub>H<sub>7</sub>N<sub>3</sub>O<sub>4</sub>PS<sub>2</sub>Br: C:27.29; H:1.78; N:10.61. Found: C:26.90; H:1.58; N:10.54.

Please substitute the following paragraph at page 238, beginning at line 13:

(48.9) 2-Amino-5-isobutyl-4-{2-[5-(O-(2-bis(N-(1-methyl-1-ethoxycarbonyl)ethyl)phosphonamido]furanyl}thiazole. mp. 142-145°C.; Anal. cald. for C<sub>23</sub>H<sub>37</sub>N<sub>4</sub>O<sub>6</sub>PS: C:52.26; H:7.06; N:10.60. Found: C: 52.21; H:6.93; N:10.62.

Please substitute the following paragraphs at page 238, beginning at line 21:

(48.11) 2-Amino-5-isobutyl-4-{2-[5-(N,N'-bis((S)-1-benzyloxycarbonyl-2-methyl)propyl)phosphonamido]furan}thiazol. Anal. cald. for ~~C<sub>35</sub>H<sub>45</sub>N<sub>4</sub>O<sub>6</sub>P-S-C<sub>35</sub>H<sub>45</sub>N<sub>4</sub>O<sub>6</sub>PS~~ + 0.5 H<sub>2</sub>O: C: 60.94; H:6.72; N: 8.12. Found: C: 61.01; H: 6.48; N: 7.82.

(48.12) 2-Amino-5-isobutyl-4-{2-[5-(N,N'-bis((S)-1-methoxycarbonyl-3-methyl)butyl)phosphonamido]furanyl}thiazole. Anal. cald. for ~~C<sub>35</sub>H<sub>41</sub>N<sub>4</sub>O<sub>6</sub>P-S-C~~: C<sub>35</sub>H<sub>41</sub>N<sub>4</sub>O<sub>6</sub>PS:C: 53.94; H: 7.42; N: 10.06. Found: C: 54.12; H: 7.62; N: 9.82.

Please substitute the following paragraphs at page 239, beginning at line 1:

(48.14) 2-Amino-5-isobutyl-4-{2-[5-(N,N'-bis((S)-1-ethoxycarbonyl-3-(S-methyl))butyl)phosphonamido]furanyl}thiazole. Anal. calcd. for ~~C<sub>23</sub>H<sub>37</sub>N<sub>4</sub>O<sub>6</sub>P-S3~~; C<sub>23</sub>H<sub>37</sub>N<sub>4</sub>O<sub>6</sub>PS3: C: 46.61; H: 6.92; N: 9.45. Found: C: 46.26; H: 6.55; N: 9.06.

(48.15) 2-Amino-5-propylthio-4-{2[5-(N,N'-(1-(S)-ethoxycarbonyl)ethyl)phosphonamido]furanyl}thiazol. Anal. calcd. for C<sub>20</sub>H<sub>31</sub>N<sub>4</sub>O<sub>6</sub>PS<sub>2</sub>: C: 46.32; H: 6.03; N: 10.80. Found: C: 46.52; H: 6.18; HN: 10.44.

(48.16) 2-Amino-5-isobutyl-4-{2-[5-(N,N'-bis((S)-1-benzoyloxycarbonyl-2-methyl)isobutyl)phosphonamido]furanyl}thiazole. Anal. calcd. for C<sub>37</sub>H<sub>49</sub>N<sub>4</sub>O<sub>6</sub>PS: C: 62.69; H: 6.97; HN: 7.90. Found: C: 62.85; H: 7.06, N: 7.81.

Please substitute the following paragraphs at page 239, beginning at line 21:

(48.19) 2-Amino-5-isobutyl-4-{2-[5-(N,N'-bis((S)-1-ethoxycarbonyl-2-phenyl)ethyl)phosphonoamido]furanyl}thiazole. Anal. calcd. for C<sub>33</sub>H<sub>41</sub>N<sub>4</sub>O<sub>6</sub>PS + 0.15 CH<sub>2</sub>Cl<sub>2</sub>: C: 59.83; H: 6.26; HN: 8.42. Found: C: 59.88; H: 6.28; HN: 8.32.

(48.20) 2-Amino-5-propylthio-4-{2-[5-(N,N'-(1-methyl-1ethoxycarbonyl)ethyl)phosphonamido]furanyl}thiazole. mp. 110-115°C: Anal. calcd. for C<sub>22</sub>H<sub>35</sub>N<sub>4</sub>O<sub>6</sub>PS<sub>2</sub> + 0.4HCl + 0.5Et<sub>2</sub>O: C: 48.18; H: 6.81; N: 9.36. Found: C: 48.38; H: 6.60; HN: 8.98.